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EXAMINER

HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/06/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/848,834

Applicant(s)

GRIMES ET AL.

Examiner

Phuong Huynh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,10-12 and 15-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 21 is/are allowed.
- 6) ☒ Claim(s) 6,10-12,15-20 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Claims 6, 10-12 and 15-22 are pending.
2. In view of the amendment filed 2/24/03, the following objection and rejections remain.
3. The drawings, filed 5/4/01, stand not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 6, 10, 15, and 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a synthetic immunogen for inducing specific antibodies against GnRH comprising SEQ ID NO: 9-20 for the production of high titers of anti-GnRH antibodies, **does not** reasonably provide enablement for (1) *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1, (2) *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1, (3) the synthetic immunogens mentioned above wherein the T-lymphocyte epitope is fused through any spacer peptide to the amino-terminus and/or carboxy-terminus of the GnRH-immunomimic peptide, (4) the synthetic immunogens mentioned above comprising an acetylated amino-terminus and/or an amidated carboxy-terminus, (5) the synthetic immunogens mentioned above wherein the promiscuous epitope is *any* "sequence of TT, DT, Malarial Protein CSP and MSP-F", (6) synthetic immunogens mentioned above wherein the spacer peptide is selected from the group consisting of SEQ IDNO: 5, 6 and 7, and (7) *any* pharmaceutical injectable composition comprising any synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino

acid sequence of SEQ ID NO: 1, or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* “promiscuous helper T-lymphocyte epitope” fused through *any* “spacer peptide” to a GnRH immunomimic peptide “comprising” a partial 2-10 amino acid sequence of SEQ ID NO: 1 and a pharmaceutically acceptable carrier for inducing specific antibodies against GnRH. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only twelve synthetic immunogens selected from the group consisting of SEQ ID NO: 9-20 for inducing specific antibodies against GnRH in animal wherein the synthetic immunogen comprises a fusion peptide consisting of a helper T peptide epitope from TT, DT, Malarial protein CSP, and MSP-F, fused to the amino terminus or the carboxy terminus of a GnRH peptide of SEQ ID NO: 1 through a spacer peptide selected from the group consisting of SEQ ID NO: 5-7. The specification discloses only one GnRH peptide of SEQ ID NO: 1.

The specification does not teach how to make and use *any* synthetic immunogen mentioned above for inducing antibodies against GnRH because the terms “promiscuous helper T-lymphocyte epitope”, “spacer peptide”, and *any* promiscuous epitope selected from *any* “sequence of TT, DT, Malarial Protein CSP and MSP-F” without SEQ ID NO have no structure, much less for inducing GnRH specific antibodies. In fact, the specification on page 4 discloses that some promiscuous helper T epitope (SEQ ID NO: 4) is not promiscuous enough to be applicable for a large number of species. Further, the term “comprising” is open-ended. It expands the immunogenic peptide of a partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acids at either or both ends of the immunogenic peptide in the claimed synthetic immunogen. There is insufficient guidance about which undisclosed amino acids to be

added and whether the resulting synthetic immunogen retains the structure that could induce specific antibodies against GnRH.

Kuby *et al*, of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed synthetic immunogen comprising the undisclosed promiscuous helper T-lymphocyte epitope fused through an undisclosed spacer sequence to any undisclosed immunogenic peptide comprising any partial 2-10 amino acid sequence of SEQ ID NO: 1 would induce GnRH specific antibody.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Abaza *et al*, of record, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed "immunomimic peptide", it is unpredictable which undisclosed synthetic immunogen comprising a helper T epitope and the undisclosed "immunomimic peptide epitope or analog thereof" would induce GnRH specific antibodies. Since the promiscuous helper T-lymphocyte epitope, the spacer peptide, the sequence of TT, DT, Malarial Protein CSP and MSP-F and the immunogenic peptide in the synthetic immunogen mentioned above are not enable, it follows that any pharmaceutical injectable composition comprising any synthetic immunogen mentioned above for inducing specific antibodies against GnRH is not enabled. Claim 10 is included in this rejection because since the structures of promiscuous T cell epitope and the GnRH peptide comprising a partial 2-10 amino acid sequence of SEQ ID NO: 1 are not enabled, the synthetic immunogen as a whole is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1-5, and 8-9 have been canceled. (2) the specification at page 7 teaches different helper T cell epitope peptides that are contiguous through a variety of spacer peptides with a GnRH-immunomimic peptide comprising either the 1-10 amino acid sequence and/or partial 2-10 amino acid sequence. (3) Newly added claim 17 overcomes the rejection of original claim 4. (4) The term "comprising" is appropriate since it would be understood not to exceed the scope of the invention as described in the instant disclosure.

However, newly added claim 17 still recite *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1 or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1. The terms "promiscuous helper T-lymphocyte epitope", "spacer peptide", and *any* promiscuous epitope selected from *any* "sequence of TT, DT, Malarial Protein CSP and MSP-F" without SEQ ID NO have no structure, much less for inducing GnRH specific antibodies. In fact, the specification on page 4 discloses that some promiscuous helper T epitope (SEQ ID NO: 4) is not promiscuous enough to be applicable for a large number of species. Further, the term "comprising" is open-ended. It expands the immunogenic peptide of a partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acids at either or both ends of the immunogenic peptide in the claimed synthetic immunogen. There is insufficient guidance about which undisclosed amino acids to be added and whether the resulting synthetic immunogen retains the structure that could induce specific antibodies against GnRH. Since the promiscuous helper T-lymphocyte epitope, the spacer peptide, the sequence of TT, DT, Malarial Protein CSP

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and MSP-F and the immunogenic peptide in the synthetic immunogen mentioned above are not enable, it follows that any pharmaceutical injectable composition comprising any synthetic immunogen mentioned above for inducing specific antibodies against GnRH is not enabled.

6. Claims 6, 10, 15, and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* “promiscuous helper T-lymphocyte epitope” fused through *any* “spacer peptide” to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1, (2) *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* “promiscuous helper T-lymphocyte epitope” fused through *any* “spacer peptide” to a GnRH immunomimic peptide “comprising” a partial 2-10 amino acid sequence of SEQ ID NO: 1, (3) the synthetic immunogens mentioned above wherein the T-lymphocyte epitope is fused through any spacer peptide to the amino-terminus and/or carboxy-terminus of the GnRH-immunomimic peptide, (4) the synthetic immunogens mentioned above comprising an acetylated amino-terminus and/or an amidated carboxy-terminus, (5) the synthetic immunogens mentioned above wherein the promiscuous epitope is *any* “sequence of TT, DT, Malarial Protein CSP and MSP-F”, (6) synthetic immunogens mentioned above wherein the spacer peptide is selected from the group consisting of SEQ IDNO: 5, 6 and 7, and (7) *any* pharmaceutical injectable composition comprising any synthetic immunogen for inducing specific antibodies against GnRH comprising *any* “promiscuous helper T-lymphocyte epitope” fused through *any* “spacer peptide” to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1, or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* “promiscuous helper T-lymphocyte epitope” fused through *any* “spacer peptide” to a GnRH immunomimic peptide “comprising” a partial 2-10 amino acid sequence of SEQ ID NO: 1 and a pharmaceutically acceptable carrier for inducing specific antibodies against GnRH.

The specification discloses only twelve synthetic immunogens selected from the group consisting of SEQ ID NO: 9-20 for inducing specific antibodies against GnRH in animal wherein the synthetic immunogen comprises a fusion peptide consisting of a helper T peptide epitope

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from TT, DT, Malarial protein CSP, and MSP-F, fused to the amino terminus or the carboxy terminus of a GnRH peptide of SEQ ID NO: 1 through a spacer peptide selected from the group consisting of SEQ ID NO: 5-7. The specification discloses only one GnRH peptide that is SEQ ID NO: 1.

With the exception of the specific synthetic immunogen mentioned above for inducing GnRH specific antibodies, there is inadequate written description about the structure, i.e. amino acid sequence associated with function of *any* "promiscuous helper T-lymphocyte epitope", *any* "spacer peptide", and *any* promiscuous epitope selected from *any* "sequence of TT, DT, Malarial Protein CSP and MSP-F" without SEQ ID NO. Further, the term "comprising" is open-ended. It expands the immunogenic peptide of a partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acids at either or both ends of the immunogenic peptide in the claimed synthetic immunogen. There is insufficient written description about which undisclosed amino acids to be added and whether the resulting synthetic immunogen retains the structure that could induce specific antibodies against GnRH. Since the promiscuous helper T-lymphocyte epitope, the spacer peptide, the sequence of TT, DT, Malarial Protein CSP and MSP-F and the immunogenic peptide in the synthetic immunogen mentioned above are not adequately described, it follows that any pharmaceutical injectable composition comprising any synthetic immunogen for inducing specific antibodies against GnRH is not adequately described. Claim 10 is included in this rejection because since the structures of promiscuous T cell epitope and the GnRH peptide comprising a partial 2-10 amino acid sequence of SEQ ID NO: 1 are not adequately described, the synthetic immunogen as a whole is not adequately described.

Finally, the specification discloses only three spacer peptides of SEQ ID NO: 5-7 and four promiscuous T helper epitopes of SEQ IDNO: 2-4 and 8 and one GnRH immunomimic peptide amino acid residues 2-10 of SEQ ID NO: 1 for the claimed synthetic immunogen, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of "promiscuous helper T-lymphocyte epitope", "spacer peptide", "sequence of TT, DT, Malarial Protein CSP and MSP-F" in the claimed synthetic immunogen to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1-5, and 8-9 have been canceled. (2) the specification at page 7 teaches different helper T cell epitope peptides that are contiguous through a variety of spacer peptides with a GnRH-immunomimic peptide comprising either the 1-10 amino acid sequence and/or partial 2-10 amino acid sequence. (3) Newly added claim 17 overcomes the rejection of original claim 4. (4) The term "comprising" is appropriate since it would be understood not to exceed the scope of the invention as described in the instant disclosure.

However, newly added claim 17 still recite *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1 or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1. With the exception of the specific synthetic immunogen mentioned above for inducing GnRH specific antibodies, there is inadequate written description about the structure, i.e. amino acid sequence associated with function of *any* "promiscuous helper T-lymphocyte epitope", *any* "spacer peptide", and *any* promiscuous epitope selected from *any* "sequence of TT, DT, Malarial Protein CSP and MSP-F" without SEQ ID NO. Further, the term "comprising" is open-ended. It expands the immunogenic peptide of a partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acids at either or both ends of the immunogenic peptide in the claimed synthetic immunogen. There is insufficient written description about which undisclosed amino acids to be added and whether the resulting synthetic immunogen retains the structure that could induce specific antibodies against GnRH. Since the promiscuous helper T-lymphocyte epitope, the spacer peptide, the sequence of TT, DT, Malarial Protein CSP and MSP-F and the immunogenic peptide in the synthetic immunogen mentioned above are not adequately described, it follows that any pharmaceutical injectable composition comprising any synthetic immunogen for inducing specific antibodies against GnRH is not adequately described.

Finally, the specification discloses only three spacer peptides of SEQ ID NO: 5-7 and four promiscuous T helper epitopes of SEQ IDNO: 2-4 and 8 and one GnRH immunomimic

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peptide amino acid residues 2-10 of SEQ ID NO: 1 for the claimed synthetic immunogen, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of "promiscuous helper T-lymphocyte epitope", "spacer peptide", "sequence of TT, DT, Malarial Protein CSP and MSP-F" in the claimed synthetic immunogen to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 6, 15 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghosh *et al* (International Immunology 11(7): 1103-1110, 1999; PTO 1449).

Ghosh *et al* teach a synthetic immunogen for inducing specific antibodies against LHRH (also known as GnRH) comprising a promiscuous helper T cell (Th) epitope such as tetanus toxin (T1) or various Th1 epitopes from E coli (T2 and T3), fused through a spacer peptide such as lysine (K) to the amino terminus (N terminus) of the immunomimic peptide LHRH such as immunogen 1 or the Carboxy terminus of the LHRH peptide such as immunogen 2 (See Fig 1, Immunogens 1 & 2, Methods, page 1107, column 1, first paragraph, Figure 1, in particular). The reference LHRH has the amino acid sequence of EHWSYGLRPG, which is identical to the claimed SEQ ID NO: 1 and amidated carboxy terminus such as LHRH-CONH₂ (See caption of Figure 1, in particular). Ghosh *et al* further teach a pharmaceutical composition comprising the reference synthetic immunogen and pharmaceutical acceptable vehicle such as PBS to produce high titers of specific anti-LHRH (antibody against GnRH) (See page 1105, page 1107, column 1, first full paragraph, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1-5, and 8-9 have been canceled. (2) the specification at page 7 teaches different helper T cell epitope peptides that are contiguous through a variety of spacer peptides with a GnRH-immunomimic peptide comprising either the 1-10 amino acid sequence and/or partial 2-10 amino acid sequence. (3) Newly added claim 17 overcomes the rejection of original claim 4. (4) The term "comprising" is appropriate since it would be understood not to exceed the scope of the invention as described in the instant disclosure. (5) The cited reference neither discloses nor suggests the presently claimed immunogen.

However, newly added claim 17 still recite *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1 or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1. Ghosh *et al* teach a synthetic immunogen for inducing specific antibodies against LHRH (also known as GnRH) comprising a promiscuous helper T cell (Th) epitope such as tetanus toxin (T1) or various Th1 epitopes from E coli (T2 and T3), fused through a spacer peptide such as lysine (K) to the amino terminus (N terminus) of the immunomimic peptide LHRH such as immunogen 1 or the Carboxy terminus of the LHRH peptide such as immunogen 2 (See Fig 1, Immunogens 1 & 2, Methods, page 1107, column 1, first paragraph, Figure 1, in particular). The reference LHRH has the amino acid sequence of EHWSYGLRPG, which is identical to the claimed SEQ ID NO: 1 and amidated carboxy terminus such as LHRH-CONH₂ (See caption of Figure 1, in particular). Ghosh *et al* further teach a pharmaceutical composition comprising the reference synthetic immunogen and pharmaceutical acceptable vehicle such as PBS to produce high titers of specific anti-LHRH (antibody against GnRH) (See page 1105, page 1107, column 1, first full paragraph, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

9. Claims 6, 15 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/25060 (Nov 1994; PTO 1449).

The WO 94/25060 publication teaches a synthetic immunogen for inducing specific antibodies against LHRH (also known as GnRH) comprising a promiscuous helper T cell (Th) epitope such as diphtheria toxin (DT), tetanus toxoid (TT), plasmodium falciparum circumsporozoite (Malarial Protein CSP) fused through a spacer peptide such as gly-Gly (GG) (See reference SEQ ID NO: 18-39, page 17, line 10-13, in particular) and a whole LHRH (also known as GnRH) immunomimic peptide that is identical to the claimed SEQ ID NO: 1 (See page 6, last paragraph, page 24, lines 30-32 through page 26, abstract in particular). The reference immunomimic peptide epitope comprises a whole GnRH sequence (See abstract, in particular). The WO 94/25060 publication further teaches a pharmaceutical composition comprising the reference synthetic immunogen and a pharmaceutically acceptable carrier (See page 29, lines 1-5, Abstract, in particular). The reference synthetic immunogen has the T helper T-lymphocyte epitope at the N-terminus since the reference LHRH (GnRH) is at the C terminus (See abstract, in particular). The reference promiscuous Th epitope provides the advantage of eliciting potent LHRH antibody responses in most members of genetically diverse population groups such as human (See page 16, line 22-25, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1-5, and 8-9 have been canceled. (2) the specification at page 7 teaches different helper T cell epitope peptides that are contiguous through a variety of spacer peptides with a GnRH-immunomimic peptide comprising either the 1-10 amino acid sequence and/or partial 2-10 amino acid sequence. (3) Newly added claim 17 overcomes the rejection of original claim 4. (4) The term "comprising" is appropriate since it would be understood not to exceed the scope of the invention as described in the instant disclosure. (5) The cited reference neither discloses nor suggests the invention as presently claimed.

However, newly added claim 17 still recite *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope"

fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1 or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1. The WO 94/25060 publication teaches a synthetic immunogen for inducing specific antibodies against LHRH (also known as GnRH) comprising a promiscuous helper T cell (Th) epitope such as diphtheria toxin (DT), tetanus toxoid (TT), plasmodium falciparum circumsporozoite (Malarial Protein CSP) fused through a spacer peptide such as gly-Gly (GG) (See reference SEQ ID NO: 18-39, page 17, line 10-13, in particular) and a whole LHRH (also known as GnRH) immunomimic peptide that is identical to the claimed SEQ ID NO: 1 (See page 6, last paragraph, page 24, lines 30-32 through page 26, abstract in particular). The reference immunomimic peptide epitope comprises a whole GnRH sequence (See abstract, in particular). The WO 94/25060 publication further teaches a pharmaceutical composition comprising the reference synthetic immunogen and a pharmaceutically acceptable carrier (See page 29, lines 1-5, Abstract, in particular). The reference synthetic immunogen has the T helper T-lymphocyte epitope at the N-terminus since the reference LHRH (GnRH) is at the C terminus (See abstract, in particular). The reference promiscuous Th epitope provides the advantage of eliciting potent LHRH antibody responses in most members of genetically diverse population groups such as human (See page 16, line 22-25, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

10. Claims 6, 15 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat NO 5,837,268 (Nov 1998; PTO 1449).

The '268 patent teaches a synthetic immunogen for inducing specific antibodies against GnRH comprising a promiscuous helper T cell (Th) epitope such as leukotoxin which is a T cell epitope having broad species reactivity (universal epitope) (See column 3, lines 10-14, in particular) fused through a spacer peptide such as an amino acid spacer group (See column 91, line 15, in particular) to a whole GnRH polypeptide that is identical to the claimed SEQ ID NO: 1 (See claims 1 and 4 of '268 patent, column 3, lines 30-54, column 6, lines 55-67, in particular). The reference helper epitope X is fused to the amino terminus and the carboxyl terminus of the

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reference GnRH (See formula GnRH-X-GnRH)_n where n is greater than or equal to 1, claims 3 and 4 of '268 patent, in particular). The reference promiscuous helper T lymphocyte epitope is fused to the amino terminus of the reference GnRH (See column 3, lines 50-53, in particular). The '268 patent teaches a pharmaceutical composition comprising the reference synthetic immunogen and a pharmaceutically acceptable vehicle such as saline (See column 16, lines 46-66, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1-5, and 8-9 have been canceled. (2) the specification at page 7 teaches different helper T cell epitope peptides that are contiguous through a variety of spacer peptides with a GnRH-immunomimic peptide comprising either the 1-10 amino acid sequence and/or partial 2-10 amino acid sequence. (3) Newly added claim 17 overcomes the rejection of original claim 4. (4) The term "comprising" is appropriate since it would be understood not to exceed the scope of the invention as described in the instant disclosure. (5) The cited reference neither discloses nor suggests the invention as presently claimed. However, newly added claim 17 still recite *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide comprising a whole amino acid sequence of SEQ ID NO: 1 or *any* synthetic immunogen for inducing specific antibodies against GnRH comprising *any* "promiscuous helper T-lymphocyte epitope" fused through *any* "spacer peptide" to a GnRH immunomimic peptide "comprising" a partial 2-10 amino acid sequence of SEQ ID NO: 1. The '268 patent teaches a synthetic immunogen for inducing specific antibodies against GnRH comprising a promiscuous helper T cell (Th) epitope such as leukotoxin which is a T cell epitope having broad species reactivity (universal epitope) (See column 3, lines 10-14, in particular) fused through a spacer peptide such as an amino acid spacer group (See column 91, line 15, in particular) to a whole GnRH polypeptide that is identical to the claimed SEQ ID NO: 1 (See claims 1 and 4 of '268 patent, column 3, lines 30-54, column 6, lines 55-67, in particular). The reference helper epitope X is fused to the amino terminus and the carboxyl terminus of the reference GnRH (See formula GnRH-X-GnRH)_n where n is greater than

or equal to 1, claims 3 and 4 of '268 patent, in particular). The reference promiscuous helper T lymphocyte epitope is fused to the amino terminus of the reference GnRH (See column 3, lines 50-53, in particular). The '268 patent teaches a pharmaceutical composition comprising the reference synthetic immunogen and a pharmaceutically acceptable vehicle such as saline (See column 16, lines 46-66, in particular). The term "comprising" is open-ended. It expands the claimed synthetic immunogen comprising the partial 2-10 amino acid sequence of SEQ ID NO: 1 to include additional amino acid at either or both ends to include the reference synthetic immunogen. Thus, the reference teachings anticipate the claimed invention.

11. The following new ground of rejection necessitated by the amendment filed 2/24/03.
12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
13. Claims 11-12, 16 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "fusion peptide" in claims 11 and 12 has no antecedent basis in base claim 17 because Base claim 17 does not recite any "fusion peptide". Base claim 17 requires a synthetic immunogen.
14. Claims 11-12 are free of prior art.
15. Claim 21 is allowed.
16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.
18. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.

Patent Examiner

Technology Center 1600

October 6, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600